

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: **Chapman and King**

Confirmation No.: **3379**

Serial No.: **09/719,045**

Art Unit: **1644**

Filed: **December 7, 2000**

Examiner: **David A. Saunders**

Title: DIVALENT ANTIBODY FRAGMENTS Customer No.: **34133**

VIA EFS Web
Filed: July 25, 2008

MAIL STOP APPEAL BRIEF- PATENTS

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

Dear Sir:

REQUEST FOR REHEARING UNDER 37 CFR § 41.52

This Request for Rehearing ("Request") is being filed in response to the Decision on Appeal dated as mailed May 27, 2008 ("Decision"). As this is being filed within two months of the Decision, it is timely.

In the Decision, the Board of Patent Appeals and Interferences ("the Board") reversed the rejection of claims 1-10, 12, 13, and 15 as anticipated by Gonzalez, but affirmed the rejections of claims 1-10, 12, 14, and 15 as obvious over Gonzalez and claims 1, 13, and 14 as obvious over Gonzalez in view of Barbanti. Appellants respectfully request reconsideration of the Decision as regards the two affirmed rejections.

Both of the affirmed rejections are based upon Gonzalez. As the Board acknowledges in the Decision, Gonzalez discloses crosslinking the polymer to the antibody through a **variety** of linkages and that, although the sulfhydryl linkage is preferred in the context of a single Fab' fragment, one would have to pick and choose among the various possible crosslinking sites to

produce a divalent antibody as claimed (Decision, p. 12, second full paragraph). Indeed, the Board acknowledged that the dumbbell-shaped structure is not precisely defined or described by Gonzalez, and admits that it can cover numerous structures where the fragments are “1) coupled via the heavy chain cysteine as in claim 1; 2) coupled via their light chains; and 3) coupled via linkages not involving the sulfhydryl group (-SH) of a cysteine residue” (Decision, paragraph bridging pp. 12-13). As further acknowledged by the Board, a variety of linkages other than sulfhydryl are described in Gonzalez, including amino, imino, carboxyl, hydroxyl, and other hydrophilic groups (Decision, p. 12, second full paragraph). As the Board is aware, all amino acids contain one or more of such groups.

While the Board found picking and choosing among a number of possibilities precluded a finding of anticipation, citing *In re Arkley*, it did not consider it to preclude a finding of obviousness. Appellants respectfully submit that the failure to find nonobviousness under the present circumstances was erroneous.

Although the standards for anticipation and obviousness differ, the number of possibilities that one needs to pick and choose from can preclude a finding of obviousness as well as a finding of anticipation. A finding of obviousness under such circumstances is essentially predicated on an “obvious to try” analysis. To find obviousness using such an analysis, the “Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. V. Teleflex Inc.*” (“the Guidelines”) require a finding that there were a **finite** number of **identified, predictable** potential solutions. Such is not true in the present case.

As noted above, the potential linkage groups that can be used are present in all amino acids. Assuming that one is beginning with an Fab’ fragment, each light chain of the fragment is

about 250 amino acids long; the portion of the heavy chain involved in the fragment is at least that long. Because the polymer can be attached to either chain, there are potentially **500** locations at which the linkage could occur **on each fragment**. Gonzalez further reports that multiple functional groups can be used to make the dumbbell-shaped structure, i.e., the linkage to each antibody does not have to be the same. The possible combinations of linkages to form the dumbbell-shaped structure is, thus, far from an identified, finite number.

In support of their affirmance, the Board alleges, *inter alia*, that the Examiner argued that Gonzalez teaches a dumbbell-shaped antibody structure comprised of two monovalent Fab' fragments (Decision at page 7). The Board is misstating the Examiner's arguments – the Examiner never argued that there were teachings of a dumbbell shaped antibody structure comprised of two monovalent Fab' fragments. Regardless, there is no teaching of such a structure in Gonzalez. Gonzalez does not specify which fragments comprise the dumbbell structure. Indeed, as the Board acknowledged, the fragments that could be involved in the dumbbell shaped structure include Fab, Fab', and F(ab')₂ (Decision, finding of fact 3). The Board is improperly reading this disclosure into the reference using Appellants' specification as a guide. This is a clear example of the inappropriate use of hindsight. *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1742, 82 USPQ2d 1385, 1397 (2007).

Appellants further maintain that Gonzalez actually teaches away from their invention – Gonzalez teaches away from having the polymer form the disulphide bridge in a divalent antibody fragment. Evidently in an attempt to counter this “teaching away,” the Board points to the discussion in Gonzalez that the invention is not limited to conjugates utilizing any particular type of linkage. First, this argument would seem to just as readily contradict the Board's reliance upon the disclosure regarding attaching the polymer to a cysteine in the hinge region of an Fab'

to support obviousness. Second, the discussion in Gonzalez regarding the avoidance of a disulphide bridge for the divalent antibody fragment is not presented merely as alternative or a preferred embodiment; Gonzalez actually discourages one of ordinary skill in the art from doing what Appellants are claiming and cannot be ignored. *See In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004).

In view of the foregoing, Appellants respectfully submit that the Board has erred in maintaining the rejections for obviousness over Gonzalez, alone or in combination with Barbanti, and request that they both be reversed.

CONCLUSION

Claims 1-10 and 12-15 are not anticipated by, or obvious over, the art cited by the Office. Appellants request that all rejections be withdrawn and that all claims be allowed.

Respectfully submitted,

/Doreen Yatko Trujillo/

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